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의학석사 학위논문

Reproducibility of calcium scoring of
the coronary arteries: Comparison
between different vendors and iterative
reconstructions

관상동맥 석회화 지수의 재현성: 제조사간
및 반복적 재구성 기법간의 비교

2017 년 2 월

서울대학교 대학원

임상의과학과

최 규 성

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최규성의 석사학위논문을 인준함

2016 년 12 월

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Abstract

Reproducibility of calcium scoring of the coronary arteries: Comparison between different vendors and iterative reconstructions

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Purpose: To assess the reproducibility of coronary artery calcium scoring performed on four different computed tomography scanners, and compare the variability between two reconstruction algorithms, filtered back projection and iterative reconstruction.

Materials and Methods: A coronary calcium scoring phantom was made from agar and contained 23 pieces of chicken bones. The phantom was scanned using four different computed tomography scanners (5 times each): Toshiba, GE, Philips, and Siemens. Images were reconstructed using the filtered back projection and iterative

reconstruction algorithms. Agatston and volume scores of total bone fragments were calculated and the overall differences between the instruments were evaluated using the Friedman test. Comparison of the Agatston and volume scores between the two reconstruction algorithms, for each instrument, was evaluated using the Wilcoxon signed rank test.

Results: The difference in the Agatston scores was significantly different between the four machines ($P = 0.001$). The Toshiba scanner yielded the highest score followed by Philips, GE, and Siemens scanners. There was no difference in the calcium scores evaluated using the two reconstruction algorithms, except in case of the Siemens scanner ($P = 0.032$).

Conclusion: Coronary calcium scores performed on different scanners varied significantly. In the Toshiba, Philips, and GE scanners, there was no significant difference in the coronary calcium score determined using either an iterative reconstruction or the filtered back projection algorithm. In the Siemens scanner, applying the iterative reconstruction algorithm resulted in a slightly different coronary calcium score (mean 9.1), which might not be clinically significant.

Keywords: iterative reconstruction; coronary artery calcium score; reproducibility; interplatform; computed tomography;

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INTRODUCTION

Coronary calcium scoring (CCS) has emerged as one of the most important methods for risk stratification and a reliable follow-up tool for coronary heart disease (1-3). In 1990, Agatston first proposed an algorithm to measure the burden of coronary calcification using electron beam computed tomography (EBCT) (4). Since then, the Agatston score has been widely used to predict the possibility of coronary artery events, such as acute myocardial infarction (5, 6).

For a method to be credible, it is crucial that the variability in measurement is as low as possible. There are several studies assessing the variability in CCS using identical machines, interscan variability, and ways to reduce this variability (7). McCollough et al. reported the standardized quantification of coronary artery calcium results from equivalent calcium scores, acquired using different computed tomography (CT) systems. (8) However, the hardware and software used in CT has improved dramatically since Agatston first proposed the Agatston score for CCS. Multi-detector channel CT (MDCT) has replaced EBCT and various reconstruction algorithms have been proposed to improve image quality. Iterative reconstruction (IR) will eventually replace filtered back projection (FBP) reconstruction as the algorithm of choice. IR enhances the CT image quality considerably and has the potential to reduce radiation dose in CT angiography for coronary artery by reducing image noise (9, 10). However, the effect of IR on CCS is yet to be evaluated.

This in vitro study has two goals; (i) To assess the variability in

CCS performed on the CT scanners from four different manufactures (Toshiba, GE, Philips, and Siemens), and (ii) To evaluate the effect of IR algorithm on CCS.

MATERIALS AND METHODS

Coronary calcium phantom

The coronary calcium phantom used in this study was made of agar and chicken bones (Fig. 1). Agar (cell-culture and electrophoresis grade) was dissolved in water (5 g in 500 ml), by heating in a regular microwave oven, and gently poured into a plastic container. On cooling, agar solidified to form a gel foam. Cooked and dried chicken bones were broken into small fragments, a few millimeters in size, with a hammer. Twenty-three bone pieces of varying size (size range, 1.4 – 6.0 mm; mean, 2.88 ± 1.06 mm) were collected and inserted into the agar gel foam using needles.

Scanning protocols

The agar phantom was scanned 5 times each using four different CT scanners (Toshiba, GE, Philips, and Siemens). The phantom was moved randomly between consecutive scans to mimic the positioning variability observed during actual patient scanning in the clinical setting. All the CT scans were performed using a sequential, and prospective acquisition. CCS was performed using manufacturer recommended protocols for each of the scanners (Table 1). The acquired CT images were reconstructed into 2.5 – 3 mm thick slices using FBP and IR algorithms, which was used for comparison. A 0.5 mm scan was acquired using the GE scanner as a reference, and the reference image was not used for comparison.

Scoring methods

CT images were analyzed using Rapidia (Infinit, Seoul, South Korea). Using images from a 0.5 mm reference scan, acquired using the GE scanner, all the bone pieces were located and serially numbered from 1 to 23. Manufacturer recommended calcium scoring protocols for each of the CT machines were used to automatically locate bone inserts, which were more than 130 Hounsfield units (HU). The Agatston score and volume score of each bone piece was measured. Calcium score of the whole phantom was defined as the sum of all the scores from individual pieces.

Comparison of calcium scores

Total calcium scores from different CT scanners and different reconstruction algorithms were compared. Friedman test was used for the overall comparison of the Agatston scores and volume scores between various CT scanners. Wilcoxon signed rank test with Bonferroni correction was performed as a post-hoc analysis. Only FBP reconstruction data was used for the comparison. Wilcoxon signed rank test was used for the comparison of the Agatston scores and volume scores between FBP and IR algorithms. All statistical analyses were performed using MedCalc software (version 16.2.1, MedCalc Software), and $P < 0.05$ was considered to be statistically significant.

RESULTS

Comparison of number of detected calcifications

Of the 23 bone pieces, only 8 to 14 pieces were detected for each scanner, since other pieces were too small and their HU values were too low to be detected. There were significant differences in detected number of bone pieces between different scanners, both with FBP and IR algorithms ($P = 0.007$, and $P = 0.013$). The Agatston score obtained from the Siemens scanner detected the least number of calcifications (Table 2) among the four vendors, with both FBP and IR algorithms. However, there were no significant differences in number of detected bone pieces for each vendor, comparing FBP and IR algorithms (all $P > 0.05$).

Comparison between different scanners

Difference in the Agatston scores and volume scores between the four CT machines was significant ($P = 0.0018$). The Toshiba scanner yielded the highest Agatston score followed by Philips, GE and Siemens scanners. The scores were significantly different in a pairwise comparison of the subgroups (Table 2, Table 3 and Fig. 2(a)). There were significant inter-vendor differences ($P = 0.003$) in the volume scores. In the pairwise comparison, there was no significant difference between GE and Philips ($P = 0.068$), and Philips and Toshiba ($P = 0.138$), while all other combinations showed significant differences ($P = 0.043$ for all comparisons) (Table 2, Table 3 and Fig. 2(b)). Agatston score differences ranged from 13.3 to 109.48 (-31.0% to +34.7% when comparing with the calcium score

from a Philips scanner, which was the median value of four machines). The differences in the volume scores were relatively smaller, ranging from 11.68 to 42.92 (−19.8% to +7.4% compared to Philips data).

Comparison between FBP and IR algorithms for different scanners

The agatston and volume scores, obtained using IR, were different for different scanners. In case of the Siemens scanner, there was an increase in the Agatston score between FBP and IR ($P = 0.032$). The mean difference was 9.1. In the Toshiba, Philips, and GE scanners, Agatston score from FBP reconstruction was comparable to that of IR. Agatston scores and volume scores for FBP and IR are shown in Table 2, and Table 3. There was an increase in the volume score, obtained from IR, in case of the Siemens and GE scanners ($P = 0.043$ for both) (Fig. 2(b)). Mean differences were 3.3 and 3.9, respectively. There was no significant difference in case of the Toshiba and Philips scanners (Fig. 2(b)).

To investigate the effect of IR in detecting tiny calcifications with low calcium scores, calcium scores of calcification observed in each of the five scans processed using FBP and IR algorithms, were averaged to obtain a Bland–Altman plot (Fig. 3). In the range of average scores < 10 , Agatston scores from IR reconstruction were significantly higher than the scores from FBP reconstruction for all scanners except Toshiba, ($P = 0.0078$ for GE, $P = 0.0156$ for Philips, $P = 0.0313$ for Siemens, and $P = 0.916$ for Toshiba). In the range of scores > 10 , Agatston scores were higher for FBP than IR for all vendors except Toshiba. However, the differences were not statistically significant ($P > 0.05$ for all comparisons). The Agatston

score from a Toshiba scanner showed a relatively higher agreement between FBP and IR when compared to the other vendors, except for an outlier with a score < 10 (Fig. 3(d)). Moreover, larger calcifications tended to show less variability and have almost identical values. Small calcifications showed larger variability (Fig. 3).

DISCUSSION

CCS is a widely accepted noninvasive tool to assess risk stratification of coronary artery events (1-3). Many studies that suggest that there are no significant differences in CCS between different CT scans, vendors, and scoring software (7, 8). However, Willemink et al. [8] recently reported that there could be significant inter-vendor variability in the Agatston scores from state-of-the-art CT machines, which can lead to inappropriate risk stratification, and re-stratification may lead to subsequent loss of early treatment (11).

Comparison of Different CT systems

In this study, we investigated the variability in calcium scoring using different CT scanners. We observed significant differences, and our result differs from the findings of McCollough et al. (8), who applied standardization at a set noise level of 20 HU for all the scanners. We did not apply any standardization in our study, which might be the reason for the observed differences. However, we followed the regular clinical protocol, which can lead to a significantly different CCS. This is in line with the recent study of Willemink et al. (11).

Several factors could affect this difference. Firstly, the number of calcifications detected can be different. In our study, the Agatston score obtained from the Siemens scanner detected the least number of calcifications (Table 2) among the four vendors, with both FBP and IR algorithms ($P = 0.007$, and $P = 0.013$). However, these undetected calcifications were very small and their total calcium score

too low to explain all the differences. Secondly, the volume difference and HU values can be other contributing factors. Volume scores are dependent solely on the number of voxels with a HU value > 130 , without considering the actual HU values of the detected calcifications (12), whereas Agatston scores are not only dependent on the lesion area occupied by calcification, but also on the HU values of calcifications (4). Though volume scores differ significantly, there is a lot more variation in the Agatston scores. This implies that the HU values may also differ with CT scanners, possibly frequently in a clinical setting, especially with state-of-the-art CT machines (11).

Also there could be an issue of risk reclassification with different vendors. In standardized categories for the CCS, patients are categorized into risk groups by using Agatston scores as follows: score of 0, absent calcification, very low risk; score of 1 - 10, minimal calcifications, low risk; score of 11 - 100, mild calcifications, intermediate risk; score of 101 - 400, moderate calcifications, moderately high risk; and score greater than 400, extensive calcifications, high risk (7, 13). Suppose there is a moderately high risk patient (Agatston scores of 101-400) who should be recommended risk factor modification and secondary prevention goals, and consider exercise testing¹³. If the patient underwent CCS with Toshiba scanner and obtained Agatston scores of 101-122, the same patient could even get Agatston scores of 0 with Siemens scanner, considering differences of Agatston score between the highest (Toshiba) and lowest (Siemens) score was 122.78. It means that there could be a reclassification as very low risk group (absent calcification) in 7.3% of moderately high risk group. Moreover, the significance of zero calcium score has been highlighted because of a

very high negative predictive value (up to 99%) for a cardiovascular events in the next 2–5 years (13, 14).

Comparison of IR and FBP reconstruction algorithms

IR has been validated in many recent studies to reduce image noise significantly, and resulted in reduction of calcium scores by reducing “blooming artifacts” (3, 13). In this study, there was very little difference in the number of calcifications detected, using IR and FBP reconstruction algorithms. The Agatston score obtained from FBP reconstruction was comparable to that of IR in three CT scanners (Toshiba, Philips and GE), and was different for only one scanner (Siemens). In a Siemens scanner, though the Agatston score obtained from FBP reconstruction was significantly higher than that obtained from IR ($P = 0.032$), the difference was relatively small (mean, 9.1) and might not be important in a clinical setting. There was no difference in the volume scores obtained using FBP and IR algorithms in case of the Toshiba and Philips scanners, and only small mean differences were observed between the Siemens and GE scanners (3.3 and 3.9, respectively). The data from the Siemens scanner shows that when the calcification is dense, which implies higher CCS, the IR results in larger scores compared to FBP reconstruction. This results in lower total Agatston or volume scores for IR compared to FBP reconstruction. This result can be explained based on the ability of IR to detect larger number of small calcifications compared to FBP reconstruction, because of lower noise. Meanwhile, if the calcification is less dense, which means lower Agatston or volume scores, IR detects more calcifications, compared to FBP reconstruction, which makes total Agatston or volume scores obtained from IR higher than that of FBP reconstruction. This result

can be explained based on the efficiency with which IR can measure smaller scores because of fewer blooming artifacts compared to FBP reconstruction. Overall, since most of the calcifications were small and less dense, total Agatston or volume scores obtained from IR were higher than the scores obtained from FBP reconstruction. Finally, the results from the Siemens scanner in our study appear to be in line with the previous study of Schindler et al. (14).

Clinical Impact

Firstly, a thorough search of published literature revealed that there were no previous studies comparing the effects of IR and FBP reconstruction algorithms for data acquired using different CT scanners. We performed a comparison to determine if significant differences exist in CCS, obtained using IR and FBP reconstruction algorithms, performed on four major CT systems: GE, Philips, Siemens, and Toshiba. As a result, there was no significant differences in CCS between IR and FBP in most vendors, which is in accordance with Schindler et al (14). There was significant difference in CCS between IR and FBP in Siemens, however the difference (mean 9.1) might not be clinically significant. Secondly, we observed significant inter-vendor differences in CCS (all $P < 0.05$). Our findings are supported by a previous study that suggests significant inter-vendor differences using FBP reconstruction, especially with state-of-art CT machines (11). Thirdly, our results from the comparison of the IR and FBP reconstruction algorithms show that the denser and larger calcifications tend to have lower CCS. On the contrary, less dense and smaller calcifications, especially with an Agatston score less than 10, which is the upper limit for minimal cardiovascular risk in risk stratification (15), tend to have higher CCS from IR than from FBP reconstruction. This is in agreement with

Schindler et al (14). However, these differences are not statistically significant. There are several limitations in this study. This is not an in vivo study. We did not use an anthropomorphic cardiac phantom with calcium insertion. Our agar phantom has a fixed amount of calcification, which makes it difficult to simulate variable calcification with variable HU values observed in clinical settings. Finally, the HU values of the phantom calcification was relatively low compared to real patients, which magnifies the observed variability and may lead to wrong risk stratification, because of the lower HU values and the more densely divided stratification.

In conclusion, CCS varied significantly between CT scanners from four different manufacturers, when evaluated using the conventional FBP reconstruction. There was no difference in the CCS obtained using IR and FBP methods in Toshiba, Philips, and GE scanners. However, in the Siemens scanner, applying the IR method resulted in a slightly higher CCS, which may not be significant in a clinical setting.

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TABLES AND FIGURES

Table 1. Computed tomography protocols used for scanning the agar coronary calcium phantom

Scanner	GE			
	MEDICAL SYSTEMS, Discovery CT750HD	Philips, Ingenuity CT	Siemens SOMATOM Definition	Toshiba, Aquilion ONE
Acquisition mode	Sequential	Sequential	Sequential	Sequential
ECG synchronization	Prospective (70%)	Prospective (70%)	Prospective (70%)	Prospective (70%)
Peak Voltage (kV)	120	120	120	120
Section thickness (mm)	2.5	3.0	3.0	3.0
Tube current (mA)	75	57	52	40
CTDI vol (mGy)	7.2	3.8	6.2	6.6
Rotation time (ms)	228	420	330	350
Reconstruction algorithm	FBP/ASIR 50%	FBP/I5	B35f/I36f	FC12n /FD12 AIDR STD

Table 2. Agatston scores evaluated from CT images acquired using four different CT scanners

	Number of detected calcifications		Agatston score	
	FBP	IR	FBP	IR
GE	12.0 \pm 1.0	12.6 \pm 1.1	153.4 \pm 7.7	157.8 \pm 6.6
Philips	11.6 \pm 0.9	11.6 \pm 0.9	166.7 \pm 4.2	166.9 \pm 3.9
Siemens	8.8 \pm 1.3	10.2 \pm 0.8	115.0 \pm 5.1	124.1 \pm 5.4
Toshiba	11.0 \pm 0.7	11.0 \pm 0.7	224.5 \pm 14.4	225.6 \pm 12.2

* FBP = Filtered back projection, IR = Iterative reconstruction

** Data are presented as mean \pm standard deviation

Table 3. Volume scores evaluated from CT images acquired using four different CT scanners

	Number of detected calcifications		Volume score	
	FBP	IR	FBP	IR
GE	11.8 \pm 1.3	12.8 \pm 1.3	143.3 \pm 8.4	146.6 \pm 8.2
Philips	11.6 \pm 0.9	11.6 \pm 0.9	157.5 \pm 6.3	156.3 \pm 5.2
Siemens	9.0 \pm 1.2	9.0 \pm 1.2	126.2 \pm 5.1	130.1 \pm 4.2
Toshiba	11.0 \pm 0.7	11.0 \pm 0.7	169.2 \pm 9.3	169.3 \pm 8.9

* FBP = Filtered back projection, IR = Iterative reconstruction

** Data are presented as mean \pm standard deviation

Figure 1. An in vitro agar phantom for coronary calcium scoring

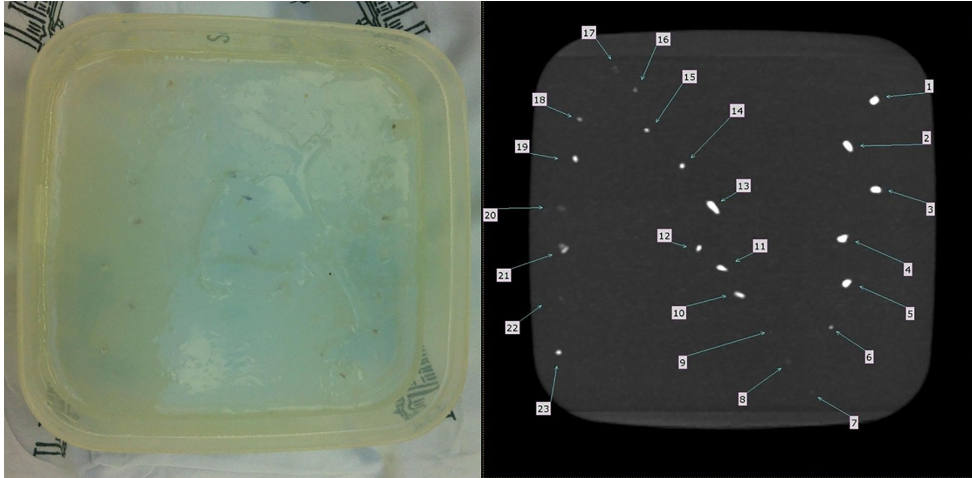
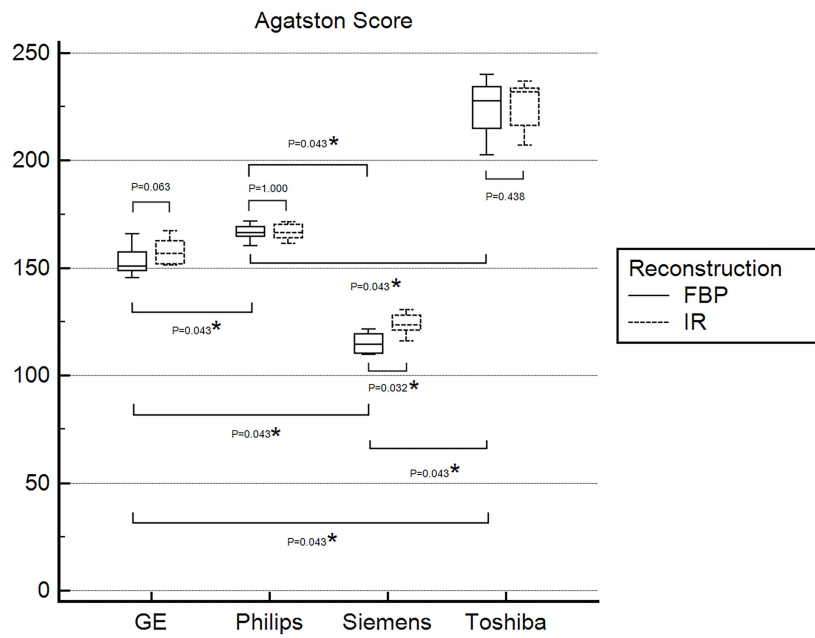


Figure 2. Comparison of (A) Agatston score and (B) volume score determined from CT images acquired using four different CT scanners (Toshiba, Philips, GE and Siemens) and following two different reconstruction algorithms (iterative reconstruction and filtered back projection).

(A)



(B)

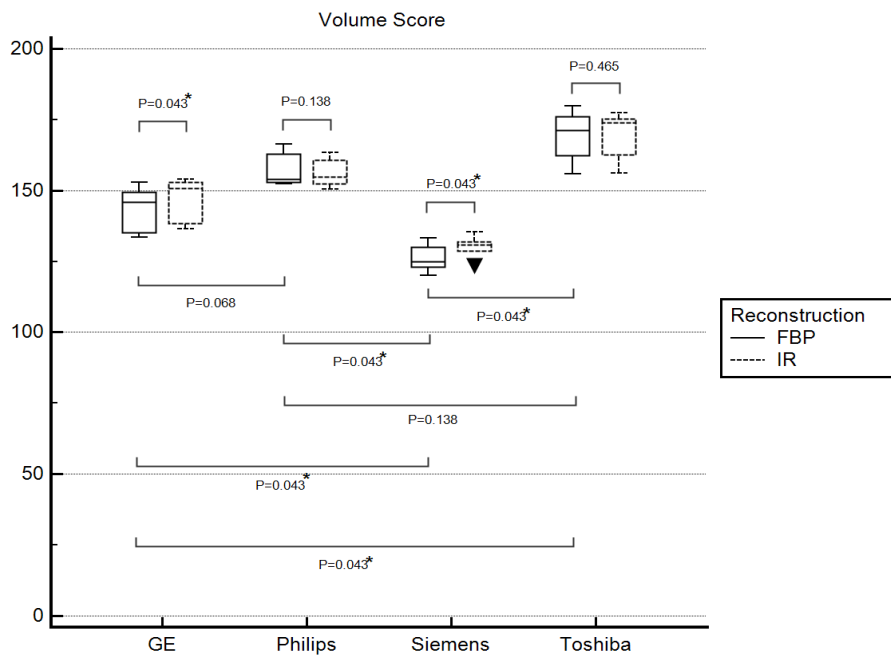
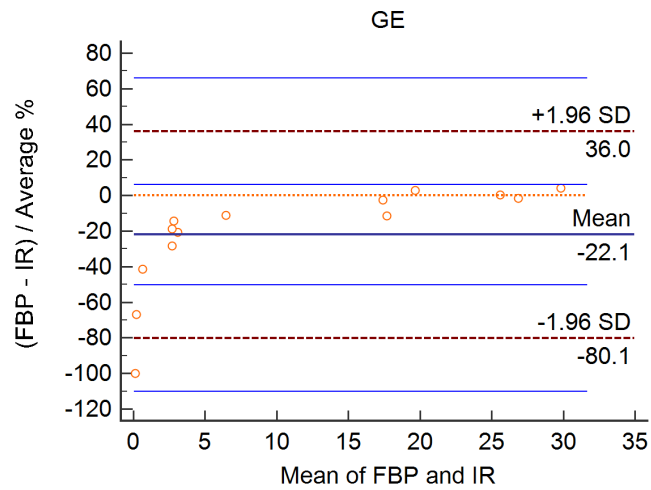
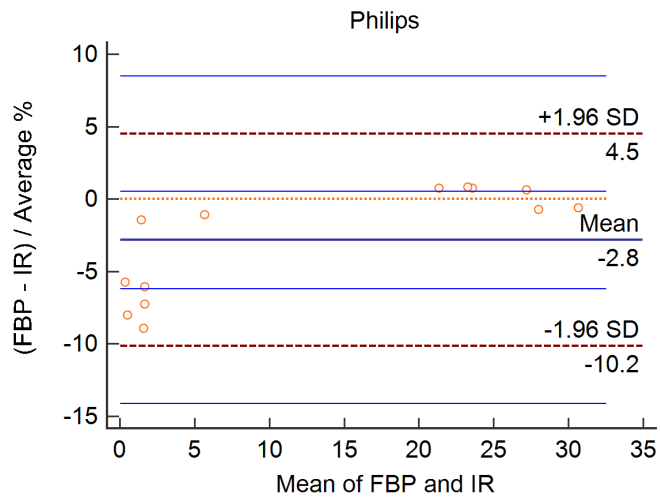


Figure 3. Bland–Altman plot comparing the two algorithms (Iterative and Filtered back projection) employed for reconstructing images acquired using (A) GE (B) Philips (C) Siemens and (D) Toshiba CT scanners. Plotted scores are averages of calcium scores for five scans for each of the calcifications

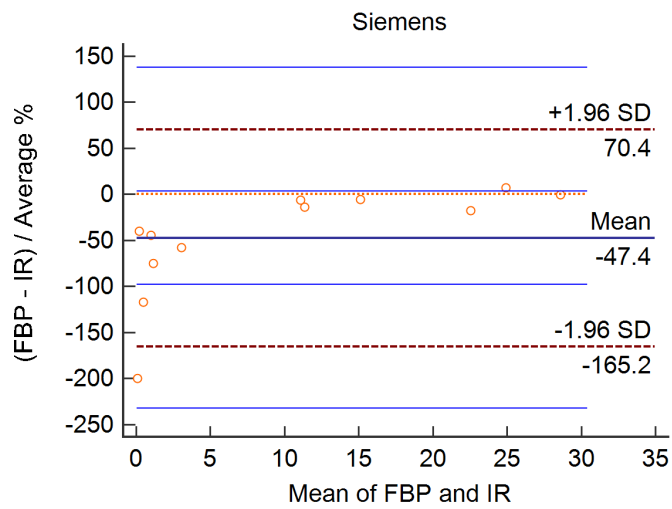
(A)



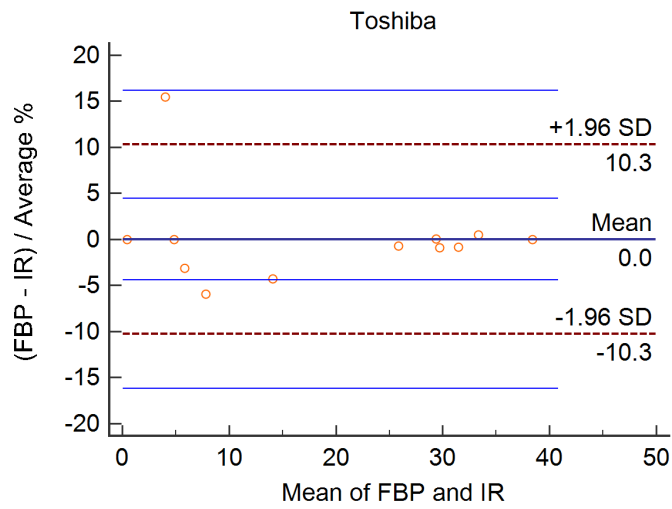
(B)



(C)



(D)



요약(국문초록)

관상동맥 석회화 지수의 재현성: 제조사 간 및 반복적 재구성 기법간의 비교

최규성

임상의학과

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본 연구는 관상동맥 석회화 지수 측정에 있어서의 제조사간의 차이 및 여과후 역투사(filtered back projection)와 반복적 재구성 기법(iterative reconstruction)간의 차이를 비교하는 연구이다.

본 연구에서는 한천과 닭뼈를 이용하여 만든 관상동맥 석회화 지수(coronary calcium scoring)측정 모형을 만들었다. 이 모형에 대해 4개의 서로 다른 제조사(Toshiba, GE, Philips, 그리고 Siemens)의 컴퓨터 단층촬영 장치를 통해 촬영을 시행하였고, 각각의 얻어진 영상정보는 여과후 역투사(filtered back projection)와 반복적 재구성 기법(iterative reconstruction)을 통해 재구성되었다. 이후 해당 제조사에서 제공하는 소프트웨어를 이용하여 Agatston 점수와 Volume 점수를 측정하였다.

이후 제조사간 점수 비교는 Friedman test를 이용하여 비교하였고, 각 제조사 내에서 재구성 기법에 따른 점수 비교는 Wilcoxon signed rank test를 이용하여 비교하였다.

그 결과, 제조사간 점수 비교에서 Agatston 점수는 유의하게 달랐다($p=0.0018$). 짝지은 비교(pairwise comparison)에서도 유의하게 차이가

났다. Toshiba, Philips, GE 그리고 Siemens 순서로 Agatston 점수가 높았다 (중앙값인 Philips를 기준으로 -31.0% ~ +34.7% 차이). Volume 점수 역시 짝지은 비교에서 GE와 Philips 그리고, Philips와 Toshiba를 제외하고는 유의하게 차이가 났다 (중앙값인 Philips를 기준으로 -19.8% ~ +7.4% 차이). 한편, 재구성 기법에 따른 비교시에도, Siemens에서는 Agatston 점수가 유의하게 차이났고, 여과후 역투사 기법보다 반복적 재구성 기법을 이용한 경우 더 증가하였다 ($p=0.032$, 평균 점수 차이 9.1). 또한, Siemens와 GE에서 Volume 점수도 유의하게 차이났고, 여과후 역투사 기법보다 반복적 재구성 기법을 이용한 경우 더 증가하였다 ($p=0.043$, 각각 평균 점수 차이 3.3 및 3.9).

결론적으로 관상동맥 석회화 지수 측정은 제조사간 점수 비교 및 재구성 기법에 따른 유의한 차이를 보였다. 하지만, 재구성 기법에 따른 차이의 경우 평균 점수 차이가 크지 않았다.

주요어: 반복적 재구성; 관상동맥 석회화 지수; 재현성; 컴퓨터 단층촬영

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